

biology and pathology, radioepidemiology, biostatistics, and radiobiology. Members shall be invited to serve for a period of one year. Management and support services shall be provided by the Office of the Director, National Institutes of Health.

"Meetings

Approximately eight meetings shall be held at the call of the chairperson who shall also approve the agenda. A government official shall be present at all meetings. Meetings shall be conducted and records of proceedings kept as required by applicable laws and Department regulations. Meetings shall be open to the public, except as determined otherwise by the Secretary; notice of all meetings shall be given to the public.

"Compensation

Members who are not full-time Federal employees shall be paid at the rate of \$100 per day, plus per-diem and travel expenses in accordance with Standard Government Travel Regulations.

"Annual Cost Estimate

Estimated annual cost for operating the Ad Hoc Working Group, including compensation and travel expenses for members but excluding staff support, is \$36,700. Estimated annual man years of staff support required is one at an estimated annual cost of \$49,213.

"Reports

Section 7(b) of Public Law 97-414 directs that within one year after the date of enactment of this Act (January 4, 1983), the Secretary of Health and Human Services shall publish the radioepidemiological tables. The Ad Hoc Working Group will complete its task as outlined in the Function section of this document and submit these findings to the Director, National Institutes of Health, by October 15, 1983.

"Termination Date

Unless renewed by appropriate action prior to its expiration, the Ad Hoc Working Group to Develop Radioepidemiological Tables will terminate on May 15, 1984.

Approved:

8-4-83

Date

(signed) Margaret M. Heckler "

Secretary

APPENDIX C: Bias associated with assuming statistical independence between estimates of dose response and estimates of modifying factors.

The magnitude of the bias can be estimated, for sites computed using approach 1 (Table IV.D.1), as follows: the inverse of the 99% upper statistical uncertainty limit (computed using lognormal assumptions) for ERR at 1 Sv is the dose, in Sv, for which the upper 99% uncertainty limit of AS is 50% ($AS = ERR/(1+ERR) = 0.5$ if $ERR = 1$). The corresponding ERR, also computed using lognormal assumptions but with the approach 2 assumption of zero covariance between $\log(\alpha)$ and $h(e, a; \gamma, \delta)$, is likely to be either higher or lower than 50%, thus indicating the direction and magnitude of bias using the decision rule selected by the DVA, and mandated by the Energy Employees Occupational Illness Compensation Program Act of 2000. The percentages of over- or under-estimation of AS using approach 2, for the five approach 1 sites, are shown in Appendix Table C.1 for exposure ages $e = 18, 20, 25$, and 30 (or over) and attained ages $a = 25, 30, 35, 40, 45$, and 50 (or over), where $a \geq e + 7$.

Approaches 1 and 2 always give the same result for $e \geq 30$ and $a \geq 50$, where ERR is assumed not to depend upon γ and δ ; otherwise, Appendix Table C.1 suggests that approach 2 usually overestimates the 99% upper limit for AS when that limit is near 50%, and apparently never underestimates it for stomach cancer among females. The non-trivial exceptions occur for liver cancer, female breast cancer, and digestive cancer among males when $e \geq 30$; they are underestimation by 0.7% to 1% (i.e., estimating the 99% upper limit for AS to be as low as 49.5% when it should be 50%) for a around 45, and underestimation by 1.3% to 2% (estimating the limit to be as low as 49% when it should be 50%) for a around 40. The correlation between $\log(\alpha)$ and δ is -0.8 or lower for the three sites with non-trivial underestimation of the 99% upper limit for AS when calculated assuming zero covariance between $\log(\alpha)$ and $h(e, a; \gamma, \delta)$, and -0.01 or higher for the other two. According to Appendix Figure C.1, only for male colon and male urinary cancer, among sites for which approach 2 was used, is the correlation between $\log(\alpha)$ and δ lower than -0.4. This suggests that downward bias of the 99% upper limit for AS by as much as 1% is a potential problem only for these two cancers, and then only for $e \geq 30$ and a around 40.

APPENDIX D: Computational Details

Uncertainty due to sampling variation

As described in Section IV, uncertainty due to statistical variation was approximated by fitted lognormal distributions for 5 site-sex combinations in Table IV.D.1 and for thyroid cancer. For other cancers it was calculated by likelihood profile distributions for the dose-response parameter, either interpolated among different values of exposure age, attained age, and/or time following exposure, or in combination with fitted lognormal uncertainty distributions for age-related modifiers of dose response. These uncertainty models were based on analyses of A-bomb survivor cancer incidence data, and were obtained for the $ERR_{I,sv}$ associated with each type of cancer.

For use in IREP, the likelihood profile distributions were specified in cumulative form by quantiles (0.25%, 0.50%, 1.25%, 2.50%, 5.00%, 12.50%, 15.85%, 50% (approximated by the maximum likelihood estimate), 84.15%, 87.50%, 95.00%, 97.50%, 98.75%, 99.50%, and 99.75%). Intermediate values were calculated by cubic spline interpolation (Press et al., 1996). For all cancer types other than leukemia, 400 interpolated points were used to define the likelihood functions. For leukemia, the $ERR_{I,sv}$ depends on both age-at-exposure and time since exposure (see below). Therefore, only one hundred interpolated points were used, in order to reduce the size of the electronic files.

To obtain the $ERR_{I,sv}$ for any age at exposure, age at diagnosis, and/or any time since exposure, linear interpolation in the logarithmic scale was performed between the tabulated $ERR_{I,sv}$ values. The $ERR_{I,sv}$ for leukemia depends on both the age-at-exposure and time-since-exposure. In this case a bilinear two-dimensional interpolation was performed (Press et al. 1996). From the numerical point of view, the cubic spline interpolation between percentiles was performed first. Then, the log-linear interpolation between ages-at-exposure or times-since-exposure was performed for each derived percentile of the likelihood function.

Phasing in the latency period

The analyses described in Section IV-C were based on a model in which the risk was assumed to be very low (or zero) for a specified minimal latency period after exposure. To avoid an abrupt jump in the ERR, we used a set of scaling factors to estimate the $ERR_{I,sv}$ for the years between the end of the latency period and the age at which maximum risk occurs.

For leukemia (all types), the latency period is considered to end 2 years after exposure, although the Life Span Study data cover only the period 5 years and more after exposure. Accordingly, we phased in the fitted ERR, allowing full expression 5 years after exposure. For 2, 3, and 4 years after exposure, the $ERR_{I,sv}$ is estimated as 0.25, 0.5, and 0.75, respectively, times the fitted value for $ERR_{I,sv}$ at 5 years after exposure.

The minimum latency period for thyroid cancer was assumed to be about 5 years, and there was no statistically significant evidence of a trend in $ERR_{I_{Sv}}$ with time following exposure. For a smooth transition, reduced values of $ERR_{I_{Sv}}$ were computed for years 3, 4, 5, 6, and 7 years after exposure by multiplying the fitted $ERR_{I_{Sv}}$ specific to each age at exposure, by 0.1, 0.25, 0.5, 0.75, and 0.9, respectively. The risk of thyroid cancer in the first three years (i.e., 0, 1, and 2) after exposure is considered to be zero.

For all other cancers, an S-shaped function similar to the one used to describe the DDREF (see the following section) was used to insure a smooth transition in $ERR_{I_{Sv}}$. The mid-point of the S-shaped function (i.e., the time since exposure at which the $ERR_{I_{Sv}}$ is half of the maximum $ERR_{I_{Sv}}$) is 7.5 years. Given the lack of precise knowledge about the on-set of different cancers, the mid-point was allowed to vary around the central value of 7.5 years after exposure. Thus, the uncertainty in the mid-point was described as a triangular distribution with a minimum of 5, a mode of 7.5 and a maximum of 10 years after the exposure. An S-shaped curve using this uncertain mid point produces a negligible $ERR_{I_{Sv}}$ for times after exposure less than 3 years and reaches the maximum $ERR_{I_{Sv}}$ at 14 years after exposure.

The dose and dose-rate effectiveness factor (DDREF)

As discussed in IV.F, for an *acute* exposure, the value $DDREF_{acute} = 1$ is used for doses larger than a randomly generated reference dose D_L , above which the dose response is assumed to be linear. As the dose approaches zero, $DDREF_{acute}$ approaches the values prescribed for chronic exposure, $DDREF_{chronic}$. The mathematical formulation for the transition from $DDREF_{acute} = 1$ at $D = D_L$ to $DDREF_{acute} = DDREF_{chronic}$ at $D = 0$, as graphed in IV.F.2, is as follows:

$$DDREF_{acute} = \begin{cases} 1 & \text{if Dose} \geq D_L \\ \frac{1}{1 - \left[\frac{1 - DDREF_{chronic}}{1 + e^{\frac{(Dose - I)}{s}}} \right]} & \text{if Dose} < D_L \end{cases}$$

The parameters I and S are, respectively, the inflection point ($I = 0.5 \times D_L$) and the “shape” parameter ($S = I/\ln(500)$); the smaller the values for S , the steeper the increase of the logistic function $1 + \exp((\text{Dose} - I)/S)$.

Note that, as the dose approaches zero, the $DDREF_{acute}$ approaches the prescribed $DDREF_{chronic}$. The value of the “shape” parameter was chosen to obtain the least steep increase of the logistic function that still reproduces the $DDREF_{chronic}$ for a zero dose¹.

¹ This relationship ensures that the DDREF for a dose equal to D_L is larger than 0.99.

Appendix E. Comparison of results from IREP with results from the 1985 NIH report and CIRRPC.

As noted in Section VI, the DVA has based its claims procedure on screening doses that were developed by CIRRPC (1988). These doses were based on the upper 99% credibility limits of the uncertainty distributions for the estimated PCs. Although the development of the screening doses was based on the 1985 NIH report, CIRRPC (1988) modified the PCs (to account for bias) and expanded the uncertainty assessment given in the original NIH report. As noted in Section VI, persons who pass the VA screening procedure usually receive an award even though CIRRPC notes that

Passing the screening criteria should not be equated with having established causality. A claim based on an exposure to radiation that just passes the screening criteria has only a very remote chance of resulting in a meritorious finding after further development of causality.

In this appendix, we compare the median ERRs from IREP with the ERRs from the 1985 NIH report, and also with the ERRs that formed the basis of the CIRRPC recommendations. We also compare the CIRRPC screening doses with those that would be obtained using the upper 99% credibility limit based on models developed in this report.

We note that CIRRPC made use of the uncertainty evaluation from the 1985 NIH publication, but modified it by adding an evaluation of statistical uncertainty, increasing the age at exposure uncertainty, and adding a positive probability of a linear dose-response in the uncertainty evaluation for the DDREF. We note particularly that the change in the DDREF uncertainty evaluation shifted the ERR distributions upward by a factor of about 1.5 for cancers other than breast and thyroid cancer, which were based on linear dose-response models with no uncertainty assumed for the DDREF. In addition, the 1985 NIH report estimated that ERRs based on Japanese atomic bomb survivors were too low by a factor of 1.62 because dosimetry revisions that eventually led to the DS86 dosimetry system had not yet been incorporated. For this reason, CIRRPC increased those ERRs that were based on atomic bomb survivor data by a factor of 1.62.

For the purpose of providing doses for screening claims, CIRRPC made the additional assumption that the claimant had a baseline risk at the 10th percentile of the distribution of the baseline risks for the cancer of interest among all counties of the United States, and the further assumption that the ERR was inversely proportional to the baseline risk. For most cancers, these two assumptions led to increasing the ERRs (and decreasing the screening doses) by a factor of 2 or more. For lung cancer, the CIRRPC screening doses for those with unknown smoking status were based on non-smokers, whereas screening doses for those who were thought to be smokers were based on those with unknown smoking status. For leukemia, CIRRPC screening doses for cases occurring less than 20 years after exposure were based on the assumption that the leukemia occurred at the

time yielding the maximum PC or ERR; for cases occurring 20 or more years after exposure, CIRRPC screening doses were based on the assumption that leukemia occurred 15 years after exposure.

Appendix Tables E.1, E.2, E.3 and E.4 are addressed at helping readers compare results based on the model described in this report (and implemented with IREP) with results based on the earlier NIH report and on CIRRPC recommendations. For each of the cancers evaluated by CIRRPC, the first three tables show ERRs for a male exposed to a chronic dose of .01 Sv at age 20 (Appendix Table E.1), age 30 (Appendix Table E.2), or age 40 (Appendix Table E.3) and developing cancer at age 50 or older. Additional scenarios are shown for leukemia. Shown in the tables are the original ERRs from NIH (1985) (column 2), modification factors used by CIRRPC (column 3), the ERRs after adjustment for these factors (column 4 in bold), and the medians of the ERR distribution generated by IREP (column 7 in bold). These three tables also show the deliberately biased CIRRPC ERRs based on the assumption of a low baseline risk (column 6).

Several factors contribute to differences in the ERRs from IREP (column 7) and the CIRRPC ERRs shown in column 4 (bold). The reader should consult Section V.C for a complete discussion of these differences. Most important, the IREP ERRs were based on cancer incidence data for the A-bomb survivors for the period 1958-87, whereas most of the NIH (1985) ERRs were based on mortality data from 1950 through 1974 or 1978. The data used by IREP include about 8600 cancers, more than twice the number evaluated earlier. For thyroid cancer, the data used by IREP were also much more extensive than those considered by NIH (1985).

The ERRs from NIH (1985) were based on age-specific absolute risk estimates, and many of these may have been statistically quite unstable, especially those for less common cancers. For most cancers, the effects of age at exposure are much stronger for NIH (1985) than IREP, and for this reason, results tend to be more comparable for older exposure ages. The NIH (1985) age at exposure effects were obtained by evaluating ratios of age-specific absolute risk estimates and age-specific baseline risks with each cancer site treated separately, whereas IREP age at exposure effects were obtained by estimating a single parameter based on all solid cancers. The longer follow-up period available for developing IREP is particularly important for evaluating the modifying effects of age at exposure, and is especially important for evaluating risks for those who were young at the time of exposure. The longer follow-up period is also important for evaluating the effects of attained age, and another reason for differences in NIH and IREP ERRs is that the latter allowed for attenuation with attained age.

Still another reason for differences is that NIH (1985) was based entirely on additive transfer between populations, whereas IREP uses an uncertain mixture of additive and multiplicative transfer, with the additive proportion uniformly weighted over the interval 0 to 1. This is especially important for cancers of the esophagus, stomach, and liver, where baseline risks are much higher in Japan than in the US population. NIH (1985) also used a strictly additive model

to account for the interaction of smoking and radiation in evaluating lung cancer risks, whereas IREP is based on a model that is intermediate between additive and multiplicative. The IREP approach decreases ERRs for smokers but increases ERRs for non-smokers as compared with the NIH (1985) approach.

Appendix Table E.4 shows the 99% screening doses from CIRRPC Table 3 for persons exposed at ages 20, 30 and 40. As noted in Section VI, the DVA has used these doses as a basis for awarding claims. Also shown (in parentheses) are the 99% screening doses that would have been obtained without the upward adjustment based on the assumption that claimants had a low baseline risk; these doses may be more appropriate for comparing with results obtained from IREP. The table also shows the doses that would yield an upper 99% confidence limit for the PC of 50% based on IREP. Unlike the results in Appendix Tables E.1, E.2, and E.3, the results in Appendix Table E.4 depend on the uncertainties in the estimated ERRs as well as the level of the ERR. The uncertainty evaluation used for IREP is considerably more comprehensive and rigorous than that used by CIRRPC. It should perhaps be noted that, for chronic exposure, the IREP screening doses are based on a linear model, whereas the screening doses from CIRRPC are based on a linear-quadratic model; in cases where the screening doses are large (small ERR), this leads to smaller CIRRPC screening doses than would have been obtained with a linear model.

APPENDIX F: Interactive RadioEpidemiological Program (IREP)

The Interactive RadioEpidemiological Program (IREP) is a web-based application that estimates the probability of causation (PC) as represented by the assigned share (AS) for an individual with a diagnosed disease who was exposed in the past to radiation. Throughout this text and online, the terms probability of causation and assigned share are used synonymously.

This program can be accessed online at the following address:

http://216.82.51.38/irep_nih

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The initial screen of the IREP user interface is shown in Figure 1. IREP has been designed to accept inputs manually or through the use of an electronic input file. To initiate a calculation, the user is instructed to click on the appropriate button.

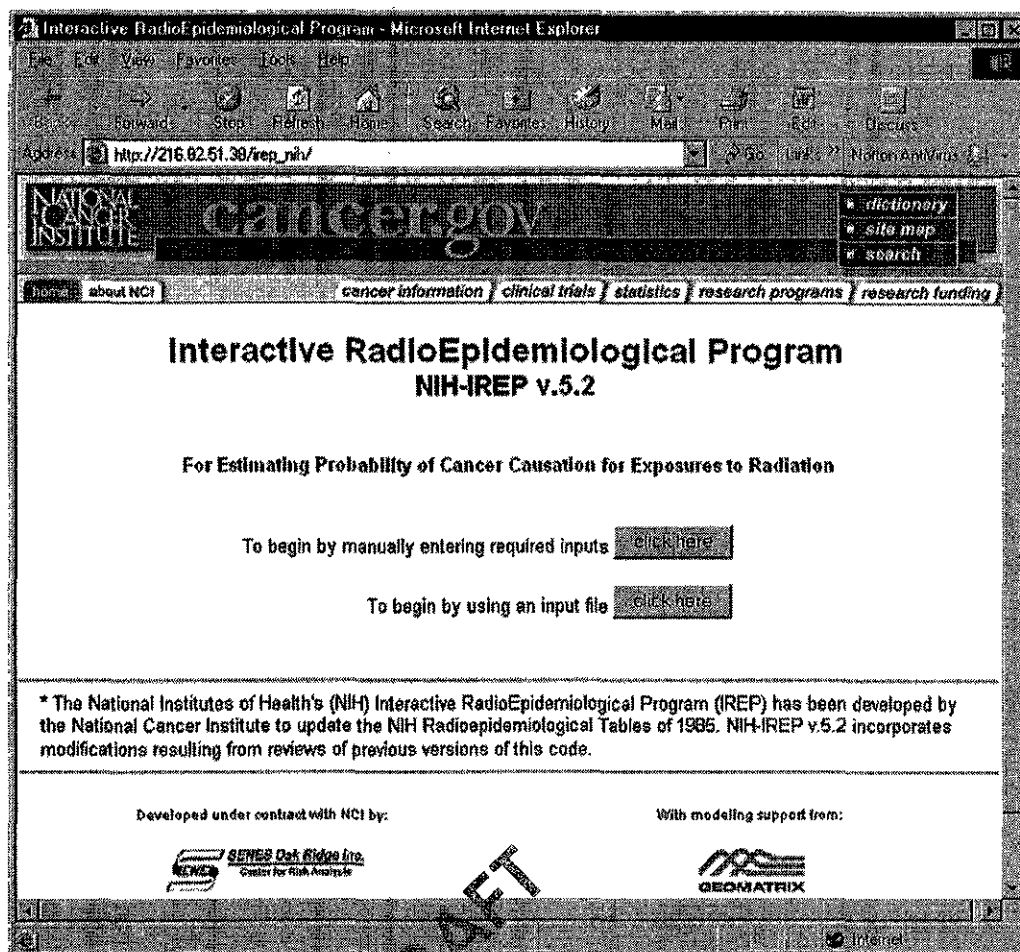


Figure 1. Initial screen of the IREP user interface

For a manual calculation using IREP, the user is requested to supply personal information (e.g. birth year, year of diagnosis, gender) and information about exposure (e.g. exposure year, organ equivalent dose, radiation type, duration of exposure). The main input screen is shown in Figure 2.

Interactive RadioEpidemiological Program - Microsoft Internet Explorer

Address: http://216.82.61.38/irep_nih/inputs1.asp

NATIONAL CANCER INSTITUTE cancer.gov

Home about NCI cancer information clinical trials statistics research programs research funding

Interactive RadioEpidemiological Program NIH-IREP v.5.2

Personal Information	Exposure Information
Name: John Q. Doe	Number of Exposures: 1
Reference ID: 123456	Dose Input Information: Enter Dose
Gender: Male	Advanced Features: Advanced Features
Birth Year: 1931	Probability of Causation: Generate Results
Year of Diagnosis: 1991	
Cancer Model: Oral Cavity and Pharynx (140-149)	
Input for Skin and Lung Cancer Only: Enter Data	

About IREP View Model Details Restart

Intermediate Results

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Figure 2. Main IREP input screen

After entering or uploading all requested input information, the probability of causation (assigned share) is estimated by a single mouse click on the button labeled "Generate Results" on the main input screen (Figure 2). The entered data will be submitted to a host computer where the underlying IREP code resides and n number of Monte Carlo iterations (using median Latin Hypercube sampling) will be performed. By default, the simulation sample size (n) is set to 1,000 iterations. The user can alter the number of Monte Carlo iterations and the initial random number seed by clicking the "Advanced Features" button located on the main input screen. The "Advanced Features" screen is shown in Figure 3.

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Interactive RadioEpidemiological Program - Microsoft Internet Explorer

Address: http://216.62.51.38/rep_nih/adv_features.asp

NATIONAL CANCER INSTITUTE cancer.gov

home about NCI cancer information clinical trials statistics research programs research funding

Interactive RadioEpidemiological Program NIH-IREP v.5.2

Enter Advanced Features Information
This page allows the user to control two sampling parameters, sample size and the random seed for sampling. This page also allows the user to override default settings for the User Defined Uncertainty Distribution.

Simulation Sample Size: Random Seed: [Generate New Random Seed](#)

User Defined Uncertainty Distribution
The User Defined Uncertainty Distribution can be adjusted to account for the presence of additional uncertainty and bias correction not presently included in IREP.
The default setting, a lognormal distribution (GM=1, GSD=1), has no effect on the calculation. Changing the default settings should only be done after sufficient justification accompanied by a written rationale.

Distribution parameters [HELP](#)

Distr Type:

[Submit Adv Data](#)

Figure 3. Advanced Features screen

A printable summary report (Figure 4) will be displayed by IREP. The report includes all input information required to estimate probability of causation.

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To gain access to additional results, the user is instructed to click the "Intermediate Results" button at the bottom of the main IREP input screen. The intermediate results provided by IREP include: absorbed dose (cGy), the radiation effectiveness factor (REF) used in the calculation, the excess relative risk, and a series of importance analyses results showing the parameters that contribute most to the overall uncertainty in the estimate of probability of causation/assigned share.

For more information about the IREP computer code and its underlying assumptions and equations, click "View Model Details" in the bar across the bottom of the main input screen (as seen in Figure 2).

Summary Report - Microsoft Internet Explorer

Address: http://216.62.51.38/irep_rnh/summ_report.asp

Interactive RadioEpidemiological Program Summary Report

Name: John Q. Doe Date of Run: 06/04/2002
Reference ID #: 123456 Time of Run: 3:52:01 PM
IREP version: 5.2

Information Used In Probability of Causation Calculation:

Gender: Male Race (skin cancer only): N/A
Birth Year: 1931 Year of Diagnosis: 1991
Cancer Model: Oral Cavity and Pharynx (140-149)
Smoking history (trachea, bronchus, or lung cancer only): N/A

IREP Assumptions and Settings:

User Defined Uncertainty Distribution: Lognormal(1,1)
Number of Iterations: 1000 Random Number Seed: 99

General Exposure Information:

Exposure #	Exposure Year	Organ Dose (cSv)	Exposure Rate	Radiation Type
1	1971	Lognormal(2,2)	chronic	electrons E<15keV

Radon Exposure Information:

N/A (applies only to cases of Lung Cancer with Radon Exposures)

PROBABILITY OF CAUSATION RESULTS:

Percentile	Probability of Causation
1st	0.00 %
5th	0.04 %
60th	0.40 %
95th	2.31 %
99th	4.05 %

Figure 4. An example of the summary report produced by IREP

To utilize the input file option, a pre-formatted electronic file is required. A standardized electronic input file can be downloaded from the Internet by selecting the input file option on the initial screen of the IREP user interface. The "Upload Saved File" screen will appear (Figure 5); click "Download Template."

Once the standardized input file is downloaded, Microsoft Excel can be used to enter the personal and exposure information in the file. After saving the modified input file (with any desired file name), the input file can be uploaded into IREP by clicking the "Browse" button.

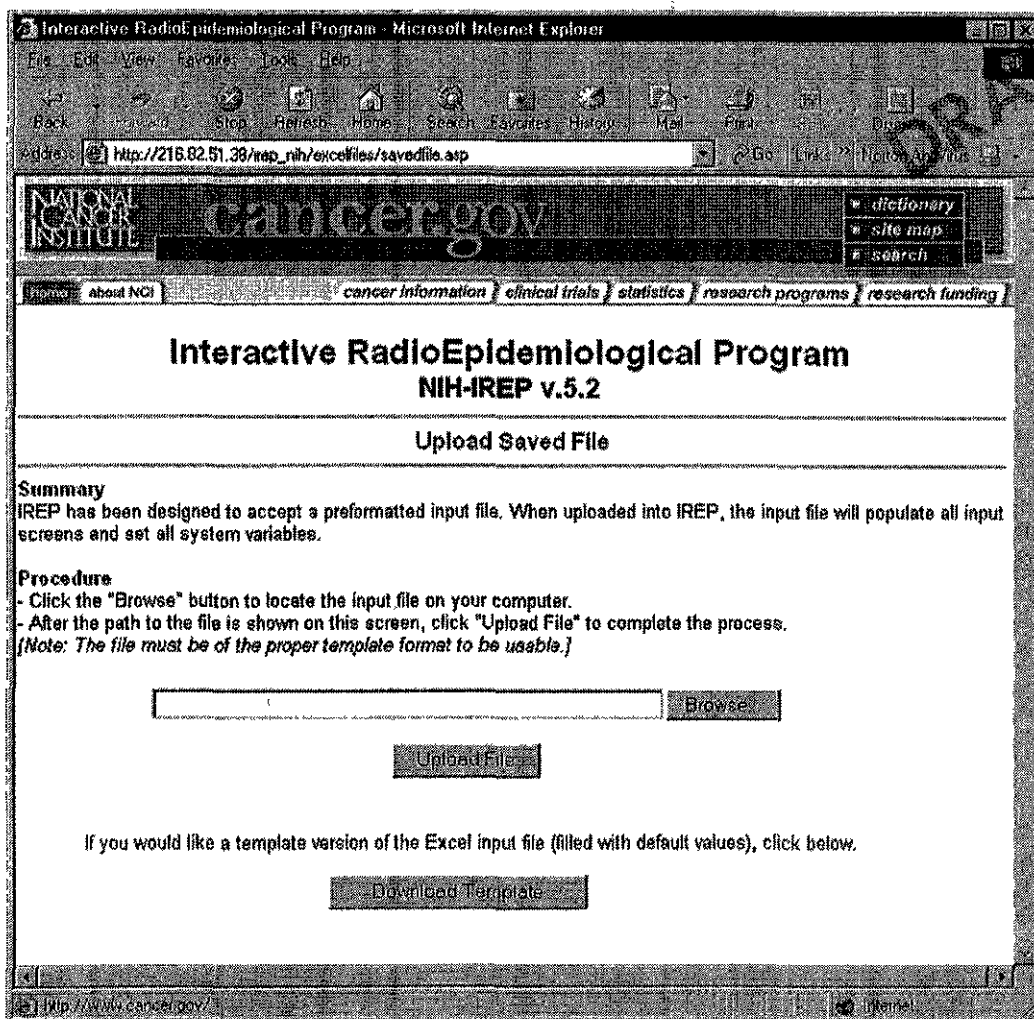


Figure 5. Upload Saved File screen

FIGURES

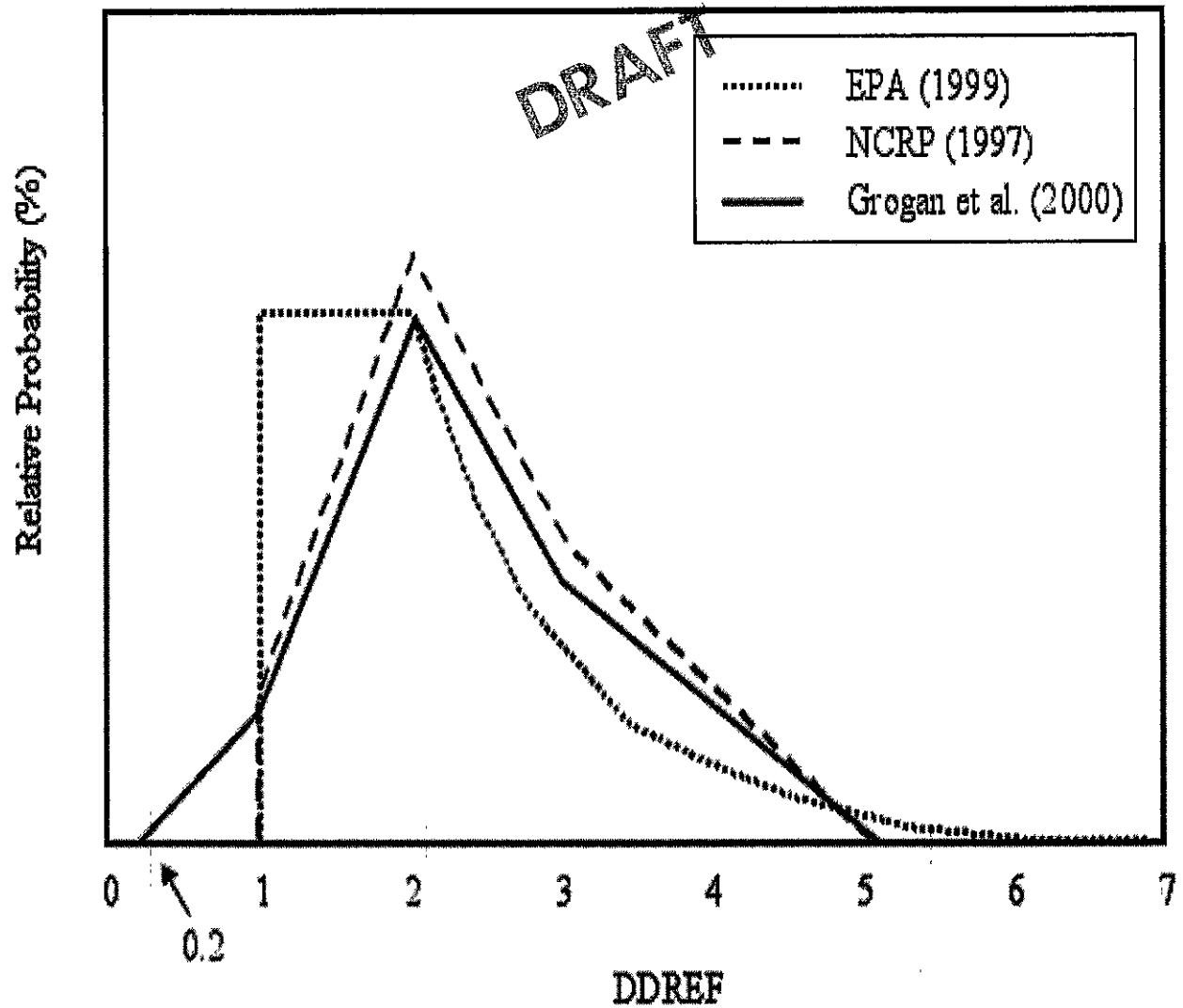
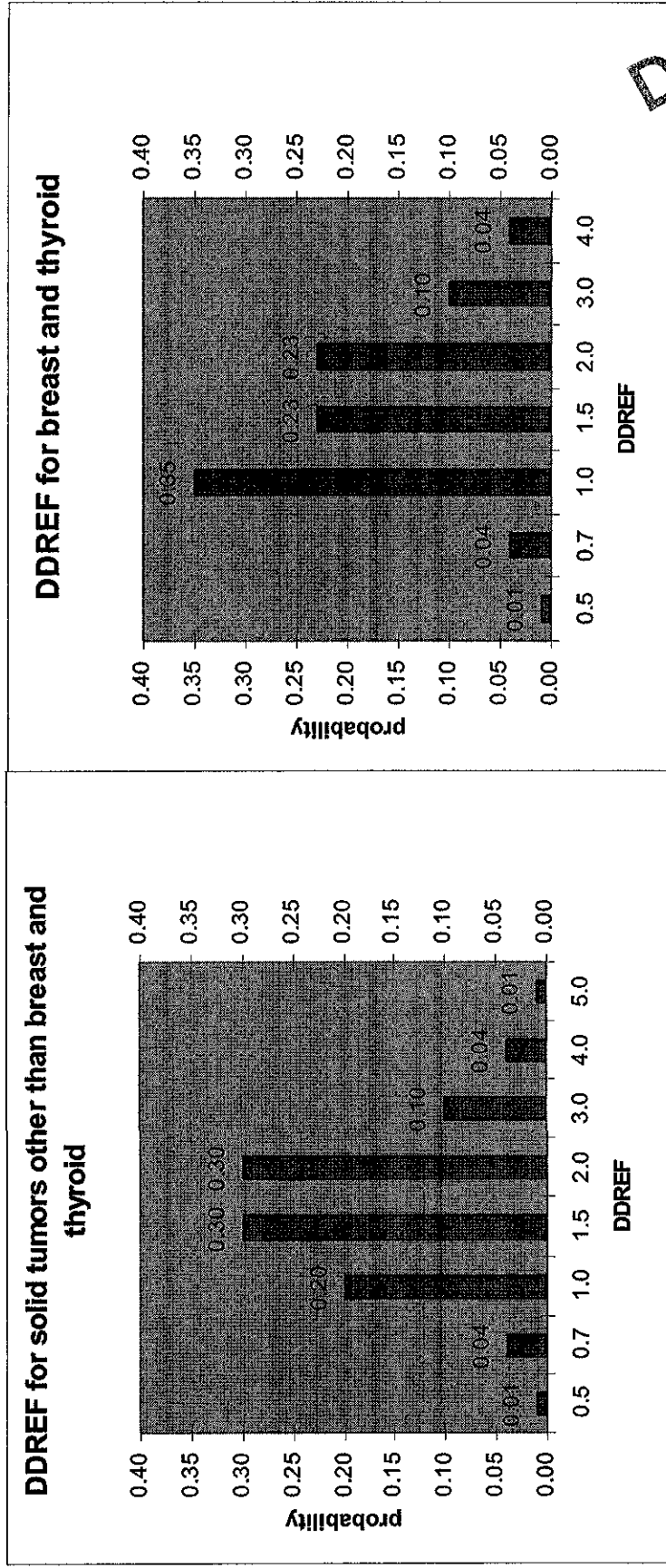


Figure IV.F.1. Probability distribution functions used by different authors to describe subjective uncertainty in the DDREF.



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Figure IV.F.2. Subjective discrete probability distributions used in this report for the dose and dose-rate effectiveness factor applied to chronic exposures, for most solid cancers (left panel), and cancers of the thyroid gland and female breast (right panel).

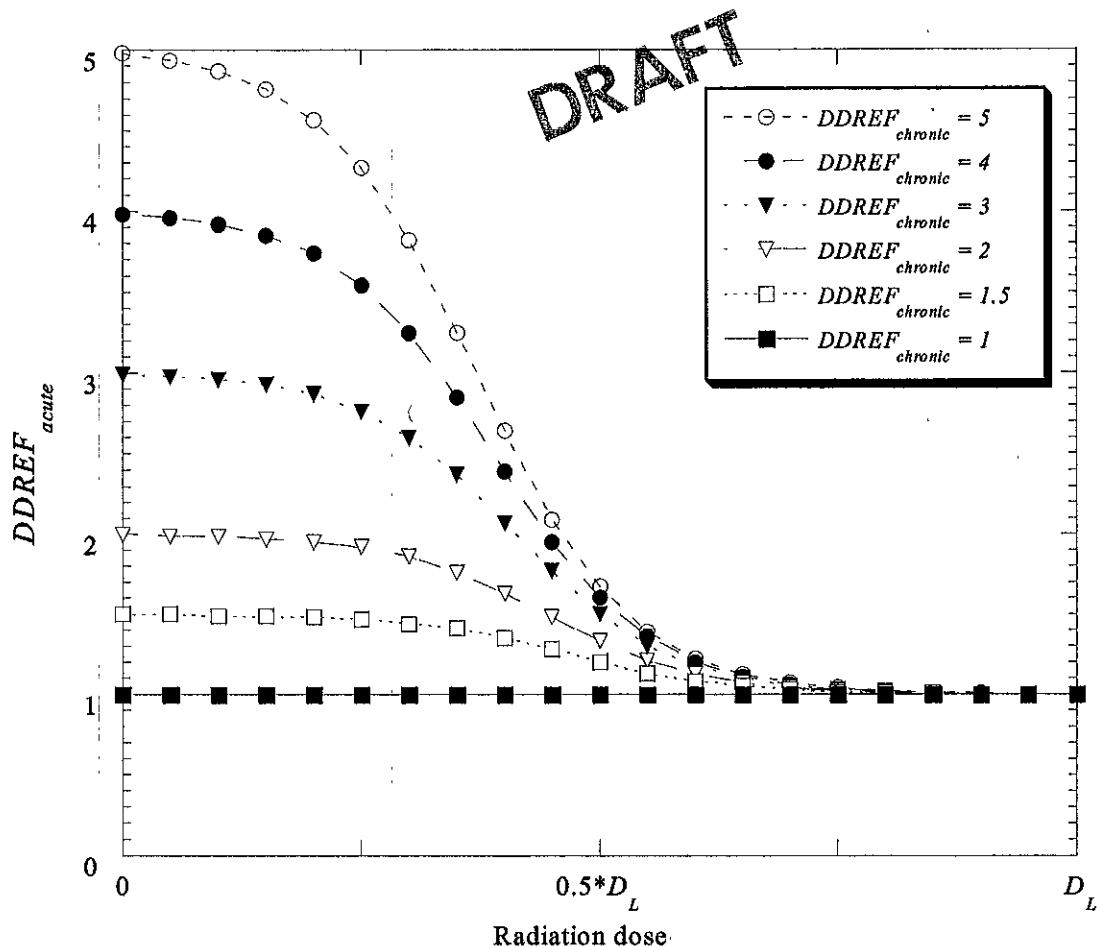


Figure IV.F.3. Variation of $DDREF_{acute}$ as a function of radiation dose for selected values of $DDREF_{chronic}$ for a fixed value of D_L , the lowest dose at which linearity of dose response is assumed to apply.

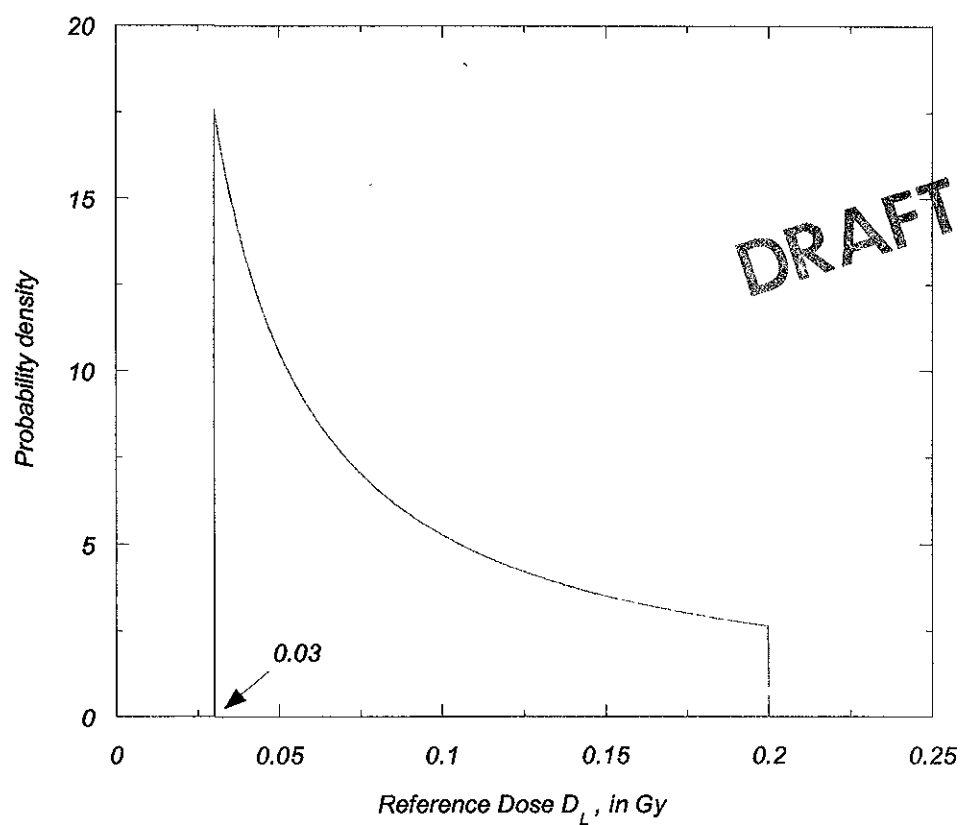


Figure IV.F.4.
Log-uniform uncertainty distribution of reference dose D_L , below which the DDREF applies.

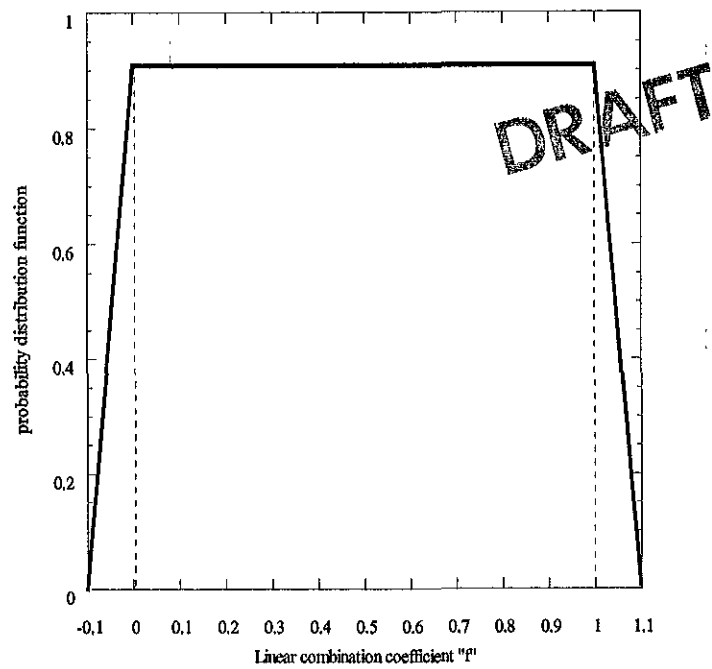


Figure IV.G.1 Probability density function assigned to the coefficient γ for linear combination of the multiplicative ($\gamma=0$) and additive ($\gamma=1$) models for transfer of excess relative risk from one population to another, for most types of cancer.

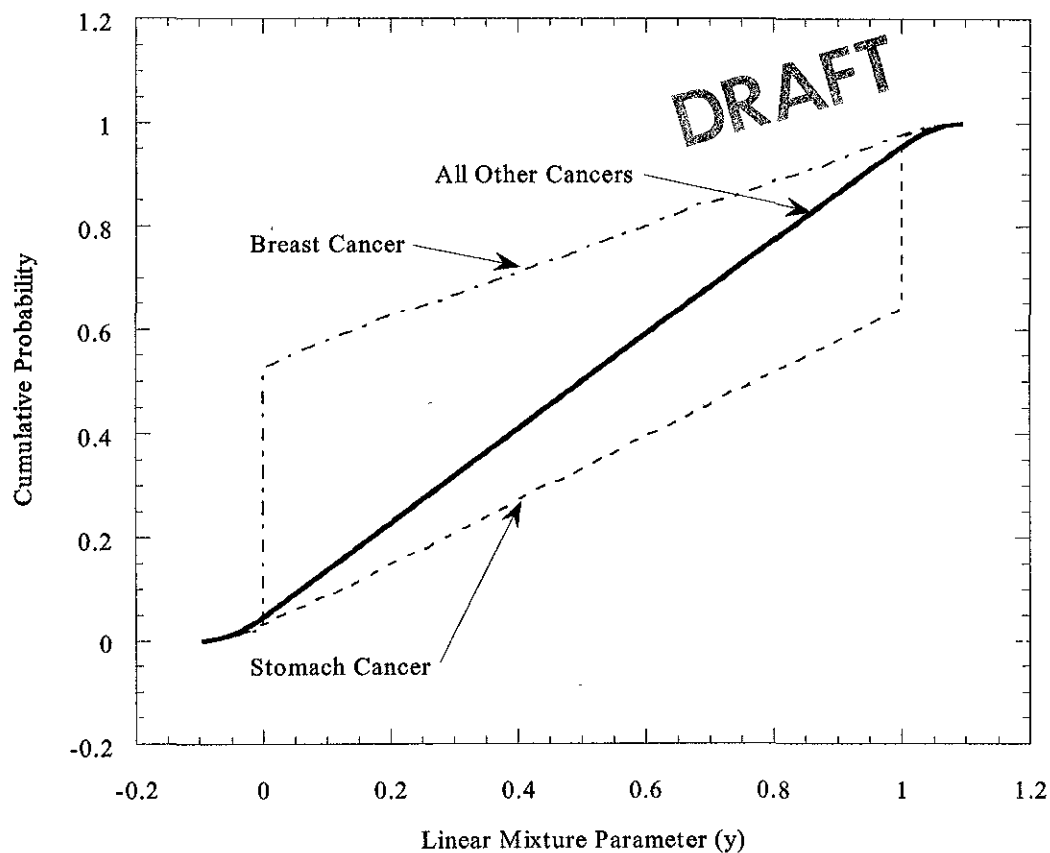
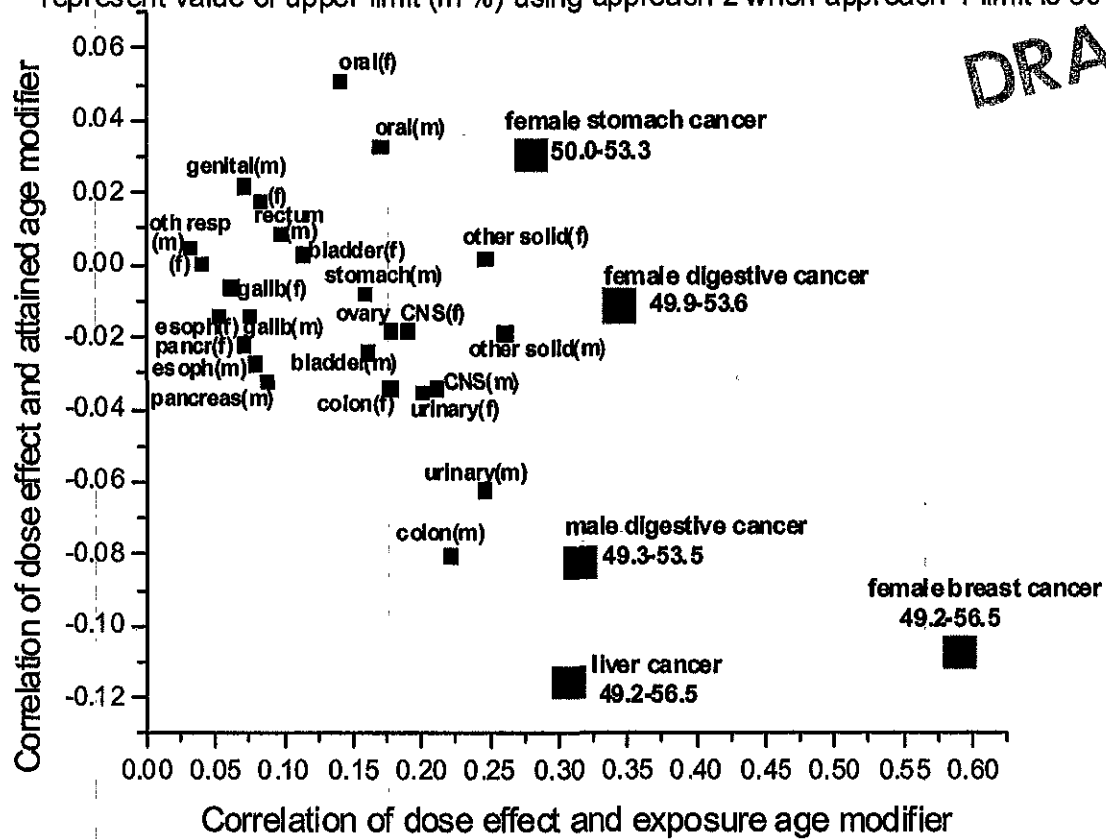


Figure IV.G.2 Cumulative distribution functions for the coefficient y used for computing a weighted average of the additive and multiplicative models for transfer between populations:

$$\text{transfer model} = y \times \text{multiplicative model} + (1-y) \times \text{additive model}.$$

Note that the transfer model for breast cancer places 50% probability on the model in Figure IV.F.1 and 50% on $y=0$, whereas for stomach cancer 33% is placed on $y=1$ and the remainder on the model in Figure IV.G.1. The multiplicative transfer model is used for thyroid cancer.

Appendix Figure C.1. Range of bias of 99% upper limit for AS, by correlation of dose and age effects. Bias ranges, given for approach 1 sites (large squares), represent value of upper limit (in %) using approach 2 when approach 1 limit is 50%.



TABLES

Table II.C.1. Cancer sites covered by the 1985 tables report.

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Site/cancer	Source of coefficients	Comments
Leukemia	BEIR III	Absolute risk coefficient for total leukemia multiplied by 0.68 for AL, 0.32 for CGL
Bone and joint	BEIR III	Injected 224-Ra only
Salivary gland	Survey of published results (Land, 1984)	Exposure ages 0-14 only
Esophagus	BEIR III	
Stomach	BEIR III	
Colon	BEIR III	Exposure ages 20+ only
Liver	BEIR III	Exposure ages 20+ only
Pancreas	BEIR III	Exposure ages 20+ only
Lung	Low-LET radiation: Kato & Schull, 1982; high-LET radiation, Jacobi et al, 1987	Exposure ages 10+ only
Breast	Tokunaga et al, 1987	Linear dose response assumed; no effect of fractionation or protraction of dose
Kidney & bladder	BEIR III	Exposure ages 20+ only
Thyroid gland	LSS incidence study (Parker et al, 1973)	Linear dose response assumed; no effect of fractionation or protraction of dose

Table IV.C.1 Solid cancer sites covered by the LSS tumor registry report (Thompson, 1994), and their treatment in the present report.

Cancer site	Organ dose used	ICD-O site codes	Number of cases		Treatment in present report
			Exposed (≥ 10 mSv)	Non-exposed (< 10 mSv)	
All solid tumors		140-165 170-195	4327	4286	Not calculated
Oral cavity and pharynx	Skin	140-149	64	68	Calculated as a group
Digestive system					
Esophagus	Stomach	150-159	2355	2442	Calculated as a group
Stomach	Stomach	150	84	101	Calculated separately
Colon	Intestine	151	1305	1353	Calculated separately
Rectum	Bladder	153	223	234	Calculated separately
Liver	Liver	154	179	172	Calculated separately
Gallbladder	Pancreas	155.0	283	302	Calculated separately
Pancreas	Pancreas	155.1, 156	143	152	Calculated separately
Other	Intestine	157	122	118	Calculated separately
		152, 158, 159	16	10	Use results for digestive system as a group
Respiratory system					
Trachea, bronchus, and lung	Lung	160-165	528	499	Not calculated
Nasal cavity	Skin	162	449	423	Calculated separately
Larynx	Lung	160	34	21	(Combined with other respiratory, non-lung cancers, and calculated as a group)
Other	Lung	161	37	43	lung cancers, and calculated as a group using lung dose)
		163-165	8	12	

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Bone	Skeleton	170		4	11	Use results for other & ill-defined sites
Skin		173		97	84	Not calculated
Melanoma		173		6	7	Not calculated
Basal cell carcinoma	Skin	173		54	26	Dale Preston, personal communication
Other non-melanoma skin ca.	Skin	173		51	41	Dale Preston, personal communication
Female breast	Breast	174		289	240	Calculated separately
Female genital		179-184		430	461	Not calculated
Ovary	Ovary	183		66	67	Calculated separately
Uterus NOS	Uterus	179		47	39	(Combined with female
Uterine cervix	Uterus	180		265	288	genital cancers other than
Uterine corpus	Uterus	182		37	48	ovary, and calculated
Other	Uterus	181, 184		15	19	as a group)
Male genital		185-187		74	86	Calculated separately [†]
Prostate	Bladder	185		61	79	(Uses risk estimates for male genital
Other	Testis	186, 187		13	7	group)
Urinary system		188-189		172	153	Calculated separately
Bladder	Bladder	188		115	95	Calculated separately
Kidney	Intestine	189.0		34	39	Uses risk estimates for urinary system
Renal pelvis and ureter	Intestine	189, 189.2		14	14	Uses risk estimates for urinary system
Other	Intestine	189.3-189.9		9	5	Uses risk estimates for urinary system
Nervous system	Brain	191, 192		69	56	Calculated separately
Thyroid	Thyroid	193		129	96	Based on data from Ron et al (1995)
Other and ill-defined sites (Residual solid cancers)	Intestine	170, 171, 175, 190, 194, 195		120	101	Calculated as a group

Table IV.C.2 Hematopoietic cancers covered by the LSS leukemia registry report (Preston, 1994), and their treatment in the present report (bone marrow dose was used for all types).

Cancer type	ICD-O site codes	Number of cases			Treatment in present report
		Exposed ($\geq 10\text{mSv}$)	Non-exposed	Total	
Leukemia, all types (except chronic lymphocytic leukemia)	204.0, 204.2 - 208	143	90	233	Calculated as a group
Acute myelogenous leukemia	205.0	60	43	103	Calculated separately
Acute lymphocytic leukemia	204.0	24	9	33	Calculated separately
Chronic myelogenous leukemia	205.1	41	17	58	Calculated separately
Lymphoma	201-202	86	105	191	Combined, and calculated as a group
Multiple myeloma	203	31	29	60	

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Table IV.D.1. Computation of uncertainty distribution for ERR at 1 Sv. 1. Sites for which lognormal theory could be used with confidence to approximate the likelihood profile distribution for $\log(\alpha)$, and for which default values of γ and δ were not used.*

Cancer site	$\log(\alpha)$	γ	δ	Var ($\log \alpha$)	Cov ($\log \alpha, \gamma$) (correlation)	Cov ($\log \alpha, \delta$) (correlation)	Var(γ)	Cov (γ, δ)	Var(δ)
All digestive Males	-1.590	-.0477	-1.622	0.10621	0.001868 (0.314)	-0.020011 (-0.082)	.0003332	-.007395	.56236
All digestive Females	-0.8614	-.0477	-1.622	0.05018	0.001403 (0.343)	-0.001882 (-0.011)	.0003332	-.007395	.56236
Stomach Females	-0.7998	-.04723	-1.781	0.07512	0.001380 (0.279)	0.006263 (0.031)	.0003252	-.007185	.54764
Liver Both sexes	-1.049	-.05204	-1.579	0.17108	0.002291 (0.307)	-0.03610 (-0.115)	.0003255	-.007347	.57368
Breast Females	0.02109	-.03722	-2.006	0.05456	0.002586 (0.589)	-0.01907 (-0.107)	.0003530	-.007934	.58018

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* For exposure age $e \geq 30$ and attained age $a \geq 50$, $\log(\text{ERR}/\text{Sv})$ is assumed to be normally distributed with mean $\log(\alpha)$ and variance $\text{Var}(\log(\alpha))$. For other values of e and a , the log scale mean and variance are:

$$\text{mean} = \log(\alpha) + \gamma \times \min[\max(-15, e-30), 0] + \delta \times \min(\ln(a/50), 0);$$

$$\text{variance} = \text{var}(\log \alpha) + 2 \times \text{cov}(\log \alpha, \gamma) \times \min[\max(-15, e-30), 0] + 2 \times \text{cov}(\log \alpha, \delta) \times \min(\ln(a/50), 0) + \text{var}(\gamma) \times \min[\max(-15, e-30), 0]^2 + 2 \times \text{cov}(\gamma, \delta) \times \min[\max(-15, e-30), 0] \times \min(\ln(a/50), 0) + \text{var}(\delta) \times \min(\ln(a/50), 0)^2$$

Table IV.D.2 Computation of uncertainty distribution for ERR at 1 Sv. 2. Likelihood profile distributions for α , for exposure age $e \geq 30$ and attained age $a \geq 50$: sites for which a lognormal approximation was not appropriate, and for which default values of γ and δ were used.*

Profile quantiles	Oral cavity and pharynx		Esophagus		Stomach		Colon		Rectum		Gall bladder		Pancreas	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
0.9975	0.8004	1.765	1.216	3.253	0.3802	1.531	1.671	0.4946	1.078	0.5258	1.114	0.7062	1.510	
0.995	0.7321	1.619	1.117	2.919	0.3516	1.429	1.567	0.4675	1.022	0.4725	1.013	0.6401	1.379	
0.9875	0.6404	1.423	0.9820	2.492	0.3137	1.289	1.423	0.3946	0.8701	0.4013	0.8761	0.5509	1.201	
0.975	0.5694	1.271	0.8755	2.179	0.2846	1.177	1.308	0.3413	0.7581	0.3465	0.7677	0.4815	1.060	
0.95	0.4962	1.113	0.7634	1.869	0.2545	1.058	1.185	0.2888	0.6467	0.2905	0.6538	0.4095	0.9117	
0.875	0.3935	0.8909	0.6025	1.450	0.2112	0.8852	1.005	0.2178	0.4917	0.2128	0.4893	0.3083	0.6984	
0.8413	0.3651	0.8288	0.5563	1.324	0.1967	0.8357	0.9537	0.1951	0.4396	0.1921	0.4442	0.2802	0.6378	
0.5	0.2055	0.4755	0.2905	0.6759	0.1184	0.5405	0.6430	0.0812	0.1875	0.0756	0.1805	0.1227	0.2871	
0.1587	0.0907	0.2136	0.0784	0.1779	0.0497	0.3020	0.3857	<0	<0	<0	<0	<0	<0	
0.125	0.0739	0.1736	0.0545	0.1229	0.0369	0.2672	0.3523	<0	<0	<0	<0	<0	<0	
0.05	0.0308	0.0724	<0	<0	0.0051	0.1694	0.2463	<0	<0	<0	<0	<0	<0	
0.025	0.0082	0.0190	<0	<0	<0	0.1134	0.1849	<0	<0	<0	<0	<0	<0	
0.0125	<0	<0	<0	<0	<0	0.0671	0.1336	<0	<0	<0	<0	<0	<0	
0.005	<0	<0	<0	<0	<0	0.0176	0.0772	<0	<0	<0	<0	<0	<0	
0.0025	<0	<0	<0	<0	<0	<0	0.0409	<0	<0	<0	<0	<0	<0	

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Profile quantiles	Respiratory, non-lung		Urinary tract		Bladder		Ovary	Male genital	Central nervous system		Residual solid cancers		Lym-phoma*
	Males	Females	Males	Females	Males	Females	Females	Males	Males	Females	Males	Females	Both sexes
0.9975	0.7400	1.716	1.480	3.561	1.561	3.887	2.02	1.51	.9370	2.006	1.504	2.989	1.600
0.995	0.7009	1.619	1.396	3.354	1.474	3.577	1.86	1.44	0.8744	1.880	1.403	2.814	1.394
0.9875	0.5725	1.319	1.281	3.071	1.312	3.172	1.65	1.23	0.7444	1.618	1.267	2.575	1.134
0.975	0.4810	1.105	1.189	2.848	1.188	2.864	1.48	1.08	0.6491	1.424	1.160	2.385	0.9465
0.95	0.3930	0.9008	1.092	2.613	1.062	2.551	1.30	0.939	0.5553	1.230	1.048	2.185	0.7651
0.875	0.2755	0.6291	0.9489	2.273	0.8843	2.115	1.05	0.733	0.4295	0.9661	0.887	1.893	0.5321
0.8413	0.2344	0.5366	0.9080	2.176	0.8311	1.987	0.982	0.667	0.3925	0.8862	0.8440	1.810	0.4742
0.5	0.0606	0.1377	0.6635	1.601	0.5388	1.282	0.576	0.3348	0.2057	0.4755	0.5859	1.315	0.1780
0.1587	<0	<0	0.4650	1.137	0.3091	0.7337	0.267	0.0670	0.0759	0.1772	0.3883	0.9148	0.0142
0.125	<0	<0	0.4380	1.073	0.2778	0.6587	0.230	0.0389	0.0600	0.1403	0.3626	0.8592	0.0032
0.05	<0	<0	0.3571	0.8820	0.1869	0.4414	0.117	<0	0.0189	.04436	0.2871	0.6946	>0
0.025	<0	<0	0.3102	0.7698	0.1352	0.3176	0.0569	<0	.00440	.01012	0.2445	0.5986	>0
0.0125	<0	<0	0.2712	0.6759	0.0925	0.2159	<0	<0	<0	<0	0.2099	0.5187	>0
0.005	<0	<0	0.2285	0.5716	0.0457	0.1057	<0	<0	<0	<0	0.1726	0.4305	>0
0.0025	<0	<0	0.2011	0.5038	0.0173	0.0393	<0	<0	<0	<0	0.1492	0.3738	>0

* For exposure age $e < 30$ and/or attained age $a < 50$, α is multiplied by the uncertain age factor $f(e, a)$, which is assumed to be independent of α and lognormally distributed. The mean and variance of $\ln(f(e, a))$, which is assumed to be normally distributed, are as follows:

$$\text{mean} = -0.05255 \times \min[\max(-15, e-30), 0] - 1.626 \times \min(\ln(a/50), 0),$$

$$\text{variance} = 0.0003261 \times (\min[\max(-15, e-30), 0])^2 - 0.007297 \times \min[\max(-15, e-30), 0] \times \min(\ln(a/50), 0) + 0.5648 \times [\min(\ln(a/50), 0)]^2.$$